Reconstruction by Pancreaticojejunostomy Versus Pancreaticogastrostomy Following Pancreatectomy Results of a Comparative Study

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Objective: To compare the results of pancreaticogastrostomy versus pancreaticojejunostomy following pancreaticoduodenectomy in a prospective and randomized setting.

Summary Background Data: While several techniques have been proposed for reconstructing pancreatico-digestive continuity, only a limited number of randomized studies have been carried out.

Methods: A total of 151 patients undergoing pancreaticoduodenectomy with soft residual tissue were randomized to receive either pancreaticogastrostomy (group PG) or end-to-side pancreaticojejunostomy (group PJ).

Results: The 2 treatment groups showed no differences in vital statistics or underlying disease, mean duration of surgery, and need for intraoperative blood transfusion. Overall, the incidence of surgical complications was 34% (29% in PG, 39% in PJ, P= not significant). Patients receiving PG showed a significantly lower rate of multiple surgical complications (P=0.002). Pancreatic fistula was the most frequent complication, occurring in 14.5% of patients (13% in PG and 16% in PJ, P= not significant). Five patients in each treatment arm required a second surgical intervention; the postoperative mortality rate was 0.6%. PG was favored over PJ due to significant differences in postoperative collections (P=0.01), delayed gastric emptying (P=0.03), and biliary fistula (P=0.01). The mean postoperative hospitalization period stay was comparable in both groups.

Conclusions: When compared with PJ, PG did not show any significant differences in the overall postoperative complication rate or incidence of pancreatic fistula. However, biliary fistula, postoperative collections and delayed gastric emptying are significantly reduced in patients treated by PG. In addition, pancreaticogastros-

tomy is associated with a significantly lower frequency of multiple surgical complications.

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reatment of the residual pancreatic cuff has always been a major problem in the reconstructive phase in pancreaticoduodenectomy (PD). Leakage and the consequent pancreatic fistula are the principal complications of PD and may be fatal. 1,2 To prevent complications following PD, several pharmacologic prophylactic approaches^{3–11} as well as various surgical techniques have been proposed that range from single closure, use of rubber or fibrin glue to occlude the main duct, pancreaticoenterostomy with the jejunum or stomach (with or without external pancreatic duct drainage, using invaginating end-to-end or end-to-side, with one or 2-layer suture or duct-to-mucosa anastomosis), and even total pancreatectomy. 1,2 With rare exceptions, 12–18 there are almost no prospective, randomized trials comparing surgical techniques. In particular, only one randomized study has been published comparing pancreaticogastrostomy (PG) versus pancreaticojejunostomy (PJ),¹² while the remaining reports are either retrospective or uncontrolled studies. 19-2

The present manuscript reports the results from 151 patients having "soft," residual pancreatic tissue and a small duct, who thus have a high risk of surgical complications, receiving either PG or PJ in a prospective, randomized fashion.

PATIENTS AND METHODS

Since 1990, a database has been used in our surgical center to prospectively register patients with periampullary neoplasms. From 2002 to October 2004, 208 PDs were performed of which 163 had a pancreas that was intraoperatively considered to be soft and had a diameter of the main duct that was less than 5 mm. All these patients were randomized to receive pancreatico–intestinal reconstruction with either PG or PJ. Ten consecutive cases operated on with a PG reconstruction before the beginning of the study were use as "learning and homogenizing" series among the 3 senior surgeons responsible of the trial (C.B., M.F., and P.P.).

Diagnostic workup consisted in abdominal ultrasonography (US) and spiral computed scan (CT). Magnetic reso-

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nance imaging (MRI) and endoscopic ultrasonography were performed in selected cases. Operative risk was evaluated on the basis of routine hematologic examinations, ECG, and pulmonary function tests.

All patients were treated with prophylactic perioperative antibiotics (intravenous gentamicin 80 mg t.i.d and metronidazole 500 mg t.i.d.). Prophylaxis for deep venous thrombosis consisted of low molecular weight heparin (0.4 mL qd) for 7 days. Octreotide at a dose of 0.1 mg was given 1 hour prior to the operation and was then given 3 times a day for 7 days.

After obtaining informed consent, the type of anastomosis was preoperatively randomized (random numbers table) to either PG or side-to-side PJ. In PG, anastomosis was carried out on the posterior wall of the stomach by a single layer with nonabsorbable interrupted stitches. The pancreas was mobilized as more as possible to be well telescoped into the gastric cavity. PJ was carried out using a single-layer pancreaticojejunal or duct to mucosa technique as previously described in a randomized, prospective trial from our institution. In the PJ group, 2 soft "easy flow" drains (12 mm; Chimed R Livorno, Italy) were routinely placed in front of and behind the pancreatic anastomosis, while a tubular silicone drain was placed in the vicinity of the hepaticojejunostomy. In the PG group, only one "easy flow" drain was placed behind the pancreatic anastomosis.

All surgical procedures were carried out by or under the supervision of experienced senior surgeons (C.B., M.F., and P.P.). An US was always performed before the discharge. All complications were prospectively collected in a database and calculated based on the number of patients. Mortality was defined as the total number of intrahospital mortalities. The definitions used to identify each abdominal complication are shown in Table 1.

The primary study endpoint was to compare the 2 groups of treatment on the base of the development of single or multiple postoperative abdominal complications.

TABLE 1. Definitions Used for Abdominal Complications

Term	Definition		
Pancreatic fistula	Any clinical significant output of fluid, rich in amylase, confirmed by fistulography		
Fluid collection	CT scan or ultrasound presence of fluid collection >5 cm in diameter with or without clinical significance		
Acute pancreatitis	At least a threefold increase of normal plasma amylase or lipase values from the 4th postoperative day confirmed by CT scan and clinical course		
Biliary fistula	Persistence of biliary drainage for more than 5 days, confirmed by fistulography		
Gastric fistula	Persistent gastric secretions for more than 5 days confirmed by the methylene blue test		
Enteric fistula	Persistent enteric secretions in the drains for more than 5 days confirmed by fistulography		
Hemorrhage	Requirement of >3 units of pRBCs (1000 mL) 24 hours after the operation		
Delayed gastric emptying	Need for nasogastric tube decompression for >10 days		

Statistical Analysis

The sample size calculation, based on the premise of improving the rate of complications (single and multiple) from 25% to 5% with alpha set at 0.05 and power of 80%, suggested a total number of 136 subjects (68 patients in each arm of the study).

Highly skewed, continuous variables were expressed with geometric means and a 95% confidence interval (CI) after logarithmic transformation. Quantitative data were assessed using a Student t test or by an ANOVA with the use of Tukey's procedure for post hoc multivariate comparison of the means. Qualitative data were compared by a χ^2 test with Yates correction or a Fisher exact test when necessary. Considering pancreatic fistulas rate (with or without other complications) and the impact on the abdominal complications of the 2 techniques as the main endpoint, our study attained a power of 0.85 and 0.87, respectively ($\alpha = 0.05$; $\beta =$ 0.2). All P values were 2-tailed, and values of P < 0.05 were considered to indicate statistical significance. Per protocol analysis was carried out. All calculations were performed with SPSS (version 11.5) statistical package (SPSS Inc., Chicago, IL).

RESULTS

Of the 163 patients that were randomized, 151 were confirmed to have a "soft" parenchyma by histology. The remaining 12 ductal cancer specimens (10 treated by PG and 2 with PJ) were found to show different degrees of fibrosis and accordingly were not considered in the present analysis, even though their inclusion did not change the final findings.

Of the 151 patients analyzed, 69 received PG and 82 were treated by PJ. In the PG group, 44 patients were male and 25 were female with a mean age of 59.3 years (95% CI, 58.2–60.4 years). In the PJ group, there were 51 males and 31 females with a mean age of 55.5 years (95% CI, 54.5–56.6 years). There were no statistically significant differences between the 2 groups. Sixty-one patients (30 in group PG and 31 in group PJ) presented with jaundice; 17 (28%) of these required placement of an endoscopic drain, while a transhepatic percutaneous approach was used in 3 cases. Preoperative diabetes was found in 17 cases (11%).

Table 2 reports the main indications for surgery. Groups PG and PJ were homogeneous with respect to the surgical technique used. Specifically, 66 of 69 patients in group PG and 70 of 82 cases in group PJ underwent a pylorus preserving procedure. There were also no statistically significant differences between the median operative times for PG or PJ, 337.2 minutes (95% CI, 336.1–338.2 minutes) and 353.9 minutes (95% CI, 352.9–354.9 minutes), respectively, and requirements for intraoperative transfusion (5 patients in each group).

The postoperative course showed 95 complications in 52 patients (34%) that included 20 patients (29%) in the PG group and 32 patients (39%) in the PJ group (P = not significant). Twenty-seven (52%) patients had more than one complication. These included 5 (25%) in group PG and 22 cases (69%) in group PJ (P = 0.002).

TABLE 2. Surgical Indications in 151 Pancreaticoduodenectomies

	Group PG (n = 69) (45.7%)	Group PJ (n = 82) (54.3%)
Ductal cancer	32 (46%)	28 (34.1%)
Ampullary carcinoma	13 (18.8%)	11 (13.4%)
Endocrine tumors	10 (14.5%)	12 (14.6%)
Intraductal papillary mucinous tumor	4 (5.8%)	10 (12.2%)
Duodenal cancer	1 (1.4%)	1 (1.2%)
Distal biliary cancer	1 (1.4%)	2 (2.4%)
Cystic tumors	1 (1.4%)	2 (2.4%)
Cystic dystrophy of the duodenal wall	1 (1.4)	9 (11%)
Other	6 (8.7%)	7 (8.5%)

PG, pancreaticogastrostomy, PJ, pancreaticojejunostomy. There were no statistically significant differences between the two groups.

The development of clinically significant pancreatic fistula was observed in 22 patients (14.5%): 9 (13%) in group PG and 13 (16%) in group PJ (P = not significant). Table 3 reports the specific complications observed.

Significant differences in favor of PG group were found regarding biliary fistula (none in PG versus 7 patients in PJ; P=0.01). Three of the 7 patients with radiologic documented biliary fistula also had associated pancreatic fistula. Significant differences were also found in fluid collections (7 in PG versus 22 in PJ; P=0.01) and delayed gastric empting (DGE) (2 in PG versus 10 in PJ; P=0.03).

The mean hospital stay was not statistically different between the 2 groups: PG, 14.2 days (95% CI, 13.1–15.3 days); PJ, 15.4 days (95% CI, 14.3–16.5 days). Overall, 10 (6.5%) patients (5 in each group) required relaparotomy. Five of these were required within 48 hours due to bleeding and 2 were due to anastomotic dehiscence (1 in each group). Three patients required a second surgical intervention to drain infected collections (1 in PG and 2 in PJ). One patient died 45 days after surgery due to progressive, acute pancreatitis of the

TABLE 3. Specific Complications Observed in 151 Cases of Pancreaticoduodenectomy

	Group PG (n = 69)	Group PJ (n = 82)	P	
Complicated patients	20 (29%)	32 (39%)	NS	
Single complication	15 (75%)	10 (31%)	0.002	
Multiple complications	5 (25%)	22 (68%)	0.002	
Pancreatic fistula	9 (13%)	13 (16%)	NS	
Biliary fistula	0	7 (8.5%)	0.01	
Enteric fistula	4 (6%)	7 (8.5%)	NS	
Pancreatitis of the cuff	1 (1.5%)	4 (5%)	NS	
Intra-abdominal fluid collection	7 (10%)	22 (27%)	0.01	
Abdominal bleeding	3 (4%)	6 (7%)	NS	
Delayed gastric empting	2 (3%)	10 (12%)	0.03	
Reoperations	5 (7%)	5 (6%)	NS	
Mortality	0	1 (1%)	NS	

PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy; NS, not significant.

cuff and complete anastomotic dehiscence leading to an overall mortality rate of 0.6%.

DISCUSSION

The safe reconstruction of pancreatic–gastrointestinal continuity after PD continues to be a challenge for the pancreatic surgeon. Despite a reduction of the mortality rate to 3%-5%, postoperative complications are still high. ^{1–32}

In controlled trials, neither the role of prophylactic medications^{3–11} nor different techniques of surgical reconstruction in preventing complications after pancreatic resections^{12–18} appear to be stated definitively. To the best of our knowledge, only 7 controlled randomized studies dealing with the comparison of different surgical techniques in the reconstruction following PD have been published. ^{12–18}

To address this issue, we compared PG (carried out on the posterior wall of the stomach by a single layer with nonabsorbable interrupted stitches) to PJ (carried out using a single layer pancreaticojejunal or duct to mucosa technique) in a prospective and randomized study. As previously described in a randomized, prospective trial from our own institution, a single layer or duct to mucosa technique in pancreaticojejunostomy shows highly similar complication rates. ¹⁶ The 2 groups in the present study were homogeneous with regards to vital statistics, underlying diseases, and operative techniques. They were also all characterized by soft residual pancreatic tissue and a main duct diameter that was less than 5 mm.

The risk of fistula formation has been shown to be directly proportional to the consistency of the residual organ by virtually all authors ^{1-2,4,5,7,12,16,25,26} and is further supported by the fact that anastomosis performed on chronic pancreatitis patients with fibrotic glands have a significantly reduced clinical incidence of complications related to anastomosis. ²⁷ In addition, the diameter of the pancreatic duct is another factor involved in the development of complications, and smaller duct size has been associated with higher risk. ^{28,29} On the basis of these considerations, in the present study the population selected for analysis was carefully chosen not only by intraoperative criteria but also on the basis of histologic findings. Thus, 12 cases with histologically established fibrosis were not included.

A previous report on 160 consecutive patients by Fabre et al²⁰ suggested that PG is a safe procedure with low mortality and morbidity. Hyodo and Nagai²¹ found that after PG the Wirsung duct is still patent and tends to dilate in the long-term. In a group of 86 patients treated by the same surgeon, Kim et al²² found a significant better early outcome using PG compared with PJ. In another nonrandomized study by Takano et al,²³ similar to a large (441 patients) but retrospective study by Schlitt et al,¹⁹ PG was found to be significantly safer than the PJ, particularly regarding the incidence of pancreatic fistula. Surprisingly, no fistula were reported in the study by Takano et al.²³ Such a trend has been recently confirmed by Oussoultzoglou et al,²⁴ who found no differences in mortality, but a significant reduction in the rate of pancreatic fistula (and related reoperations) and the dura-

tion of hospital stay in favor of PG reconstruction in 250 patients analyzed retrospectively.

The only prospective randomized trial available up to now comes from the John Hopkins group, ¹² which did not confirm the findings of previous uncontrolled studies. The present study is only the second randomized trial comparing the 2 reconstructive techniques. In accordance with the results reported by Yeo et al, ¹² we did not reveal any significant differences between PG and PJ either of the overall rate of complications (29% versus 39%, respectively) or in the incidence of pancreatic fistula (13% versus 16%, respectively).

The overall number of patients and composition (n = 145; 73 PG, 72 PJ) in the study published by Yeo et al¹² is comparable to the present one. Moreover, the overall incidence of pancreatic fistula is also similar in the 2 studies (14. 5% versus 12%), even when grouped according to surgical reconstruction technique [(PG, 13% versus 12%) and PJ (16% versus 11%)]. Taken together, this does not support the hypothesis that PG is safer than PJ as suggested by the uncontrolled studies.

Despite this major conclusion, when examining the single complications reported in Table 3, some significant differences can be found that favor the use of PG. Biliary fistulae, for example, were not present in the PG group, while 7 were arose in patients treated with PJ. This difference might be related to the presence in a nearby area of a double (jejunal-pancreatic and biliary) anastomosis in PJ versus a single biliary anastomosis in PG. This justification appears to be confirmed by the observation that in 3 of 7 patients with radiologically documented biliary fistula also had concomitant pancreatic fistula. Also, the presence of a single drain in PG versus 2 drains in PJ could theoretically contribute to this difference.

Moreover, the fluid collections rate was significantly lower in the PG group. Considering our definition (detection of a collection of >5 cm in diameter by US or CT with or without clinical significance), it is important to underline that, in 12 of 22 patients in the PJ group with this complication, no clinical signs were detectable. As expected, 10 patients in PJ group with multiple symptoms experienced DGE. The lower rate of collection in PG can be related to the smaller post-surgical anatomic peri-anastomotic space remaining compared with PJ; the intimate proximity of the stump to the posterior wall of the stomach allows a tension-free, wide, and well-suitable anastomosis with adequate tissue to "telescope" the stump into the gastric cavity.

The gastric acid environment is thought to inhibit the activation of pancreatic enzymes. This consideration, together with the lower tendency for ischemia due to the rich gastric vascular supply, probably justifies the trend (P = not significant) toward a lower rate of pancreatitis of the cuff in the PG group (1.5% versus 5%).

Even if a significant reduction in the overall rate of complications between the 2 groups was not observed, taken together all the aforementioned factors (lower rate of biliary fistula, collections, DGE, and pancreatitis of the cuff) contribute to a significantly lower incidence of cases with multiple complications (25% PG versus 69% PJ, P=0.002).

Thus, we conclude that PG is a safe and valid alternative to PJ and leads to a lower risk of multiple complications.

With PG reconstruction after a pylorus preserving PD, a theoretical problem exists: an active pyloric sphincter can lead to gastric obstruction and anastomotic leakage, although this has never clearly demonstrated. However, in our experience, the patients with DGE in the PG group had associated pancreatic fistula with highly severe clinical impact (mixed pancreatic and gastric fistula). Accordingly, the intraoperative dilation of the pyloric sphincter²⁵ and the possibility for maintaining a nasogastric tube for longer periods of time in patients with PG reconstruction should be considered.

The overall mortality rate (0.6%) and reoperation rate (6.5%) in the present trial also permit the conclusion that, at least in our hands, PD is still a demanding procedure, but with a medium to low risk.²⁵

At present, the only reproducible factor able to significantly reduce the morbidity and mortality rate in pancreatic resections appears to be the establishment of high-volume, regional centers (and surgeons!). In specialized centers, the "know how" for both PG and PJ should be available and the techniques to be adopted should be chosen based on the characteristics of individual cases. PG should be considered whenever anatomic conditions make anastomosis easier, safer, more tension-free, and more suitable to avoid discrepancy in size with pancreatic remnants.

CONCLUSION

On the basis of the results of our controlled, randomized trial, compared with PJ, PG following PD does not significantly change the risk of overall complications or the incidence of pancreatic fistula. However, significant decreases in the risk of associated complications, biliary fistulas, postoperative collections, and DGE were observed using PG.

REFERENCES

- Alexakis N, Halloran C, Raraty C, et al. Current standard of surgery for pancreatic cancer. Br J Surg. 2004;91:1410-1427.
- Sakorafas GH, Friess H, Balsiger BM, et al. Problems of reconstruction during pancreatoduodenectomy. *Dig Surg*. 2001;18:363–369.
- Yeo CJ, Cameron JL, Lillemoe KD, et al. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. *Ann Surg.* 200;232:419–429.
- Buchler M, Friess H, Klempa I, et al. Role of octreotide in the prevention of postoperative complications of elective pancreatic resection. *Am J Surg*. 1992;163:125–131.
- Pederzoli P, Bassi C, Falconi M, et al. Efficacy of octreotide in the prevention of complications of elective pancreatic surgery: Italian Study Group. Br J Surg. 1994;81:265–269.
- Montorsi M, Zago M, Mosca F, et al. Efficacy of octreotide in the prevention of pancreatic fistula after elective pancreatic resections: a prospective, controlled, randomized clinical trial. *Surgery*. 1995;117: 26–31.
- Friess H, Beger HG, Sulkowski U, et al. Randomized controlled multicentre study of the prevention of complications by octreotide in patients undergoing surgery for chronic pancreatitis. *Br J Surg*. 1995;82:1270–1273.
- Lowy AM, Lee JE, Pisters PW, et al. Prospective, randomized trial of octreotide to prevent pancreatic fistula after pancreaticoduodenectomy for malignant disease. *Ann Surg.* 1997;226:632–641.
- Gouillat C, Chipponi J, Baulieux J, et al. Randomized controlled multicentre trial of somatostatin infusion after pancreaticoduodenectomy. Br J Surg. 2001;88:1456–1462.

- Sarr MG for the Pancreatic Surgery Group. The potent somatostatin analogue vapreotide does not decrease pancreas-specific complications after elective pancreatectomy: a prospective, multicenter, double-blinded, randomized, placebo-controlled trial. *J Am Coll Surg.* 2003;196:556–565.
- Suc B, Msika S. Piccinini M, et al. Octreotide in the prevention of intra-abdominal complications following elective pancreatic resection: a prospective, multicenter randomized controlled trial. *Arch Surg.* 2004; 139:288–294.
- Yeo C, Cameron J, Maher M, et al. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. *Ann Surg.* 1995;222:580–588.
- Reissman P, Perry J, Cuenca A, et al. Pancreaticojejunostomy versus controlled pancreaticocutaneous fistula in pancreaticoduodenectomy for periampullary carcinoma. Am J Surg. 1995;169:585–588.
- Tran K, Van Eijck C, Di Carlo V, et al. Occlusion of the pancreatic duct versus pancreaticojejunostomy: a prospective randomized trial. *Ann Surg.* 2002;236:422–428.
- Strasberg SM, Debrin JA, Mokadam NA, et al. Prospective trial of a blood supply-based technique of pancreaticojejunostomy: effect on anastomotic failure in the Whipple procedure. J Am Coll Surg. 2002; 194:746–758.
- Bassi C, Falconi M, Molinari E, et al. Duct-to-mucosa versus end-to-side pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: results of a prospective randomized trial. Surgery. 2003;134:766–771.
- Suc B, Msika S, Fingerhut A, et al. Temporary fibrin glue occlusion of the main pancreatic duct in the prevention of intra-abdominal complications after pancreatic resection: prospective randomized trial. *Ann* Surg. 2003;237:57–65.
- Lillemoe KD, Cameron JL, Kim MP, et al. Does fibrin glue sealant decrease the rate of pancreatic fistula after pancreaticoduodenectomy? Results of a prospective randomized trial. *J Gastrointest Surg.* 2004;8: 766–764.
- Schlitt HJ, Schmidt U, Simunec D, et al. Morbidity and mortality associated with pancreatogastrostomy and pancreatojejunostomy following partial pancreatoduodenectomy. Br J Surg. 2002;89:1245–1251.
- Fabre JM, Arnaud JP, Navarro F, et al. Results of pancreatogastrostomy after pancreaticoduodenectomy in 160 consecutive patients. Br J Surg. 1998;85:751–754.
- Hyodo M, Nagai H. Pancreatogastrostomy after pancreatoduodenectomy with or without duct-to-mucosa anastomosis for the small pancreatic duct: short and long term results. *Hepatogastroenterology*. 2002;47: 1138–1141.
- Kim SW, Youk EG, Park YH, et al. Comparison of pancreaticogastrostomy and pancreaticojejunostomy after pancreaticoduodenectomy performed by one surgeon. World J Surg. 1997;21:640–643.
- Takano S, Ito Y, Watanabe Y, et al. Pancreaticojejunostomy versus pancreaticogastrostomy in reconstruction following pancreaticoduodenectomy. Br J Surg. 2000;87:423–427.
- Oussoultzoglou E, Bachellier P, Bogourdan JM, et al. Pancreaticogastrostomy decreased relaparotomy caused by pancreatic fistula after pancreaticoduodenectomy compared with pancreaticojejunostomy. *Arch Surg.* 2004;139:327–335.
- Bassi C, Falconi M, Salvia R, et al. Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients. *Dig Surg.* 2001;18:453–457.
- Bartoli FG, Arnone GB, Ravera G, et al. Pancreatic fistula and relative mortality in malignant disease after pancreaticoduodenectomy: review and statistical meta-analysis regarding 15 years of literature. *Anticancer Res.* 1991;11:1831–1148.
- Friess H, Malfertheiner P, Isenmann R, et al. The risk of pancreaticointestinal anastomosis can be predicted preoperatively. *Pancreas*. 1996; 13:202–208.
- Al-sharaf K, Ihse I, Dawiskiba S, et al. Characteristic of the gland remnant predict complications after subtotal pancreatectomy. *Dig Surg*. 1997;14:101–106.
- Hamanaka Y, Nishihara K, Hamasaki T, et al. Pancreatic juice output after pancreatoduodenectomy in relation to pancreatic consistency, duct size, and leakage. Surgery. 1996;119:281–287.
- Van Geen RC, Gouma DJ. Impact of hospital volume on in-hospital mortality in pancreatic surgery. Surg Technol Int. 2002;10:61–65.
- 31. Saettler EB, Temple WJ. The surgeon as a prognostic factor in the

- management of pancreatic cancer. Surg Oncol Clin North Am. 2000;9: 133–142
- 32. Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med*. 2002;346:1128–1137

Discussions

Dr. Russell: Thank you very much, Dr. Bassi. I enjoyed both reading the paper and hearing your exposition. Many studies have been performed comparing pancreatogastrostomy with a pancreatojejunal anastomosis, but most of these papers have not had the quality protocol of your study or that of the Hopkins group to which you refer. Your main conclusion, combined with that of the study from Baltimore, is that there is no real difference between the 2 techniques. Of course, the results you present favor the gastric anastomosis simply because there are fewer multiple complications with that technique. Indeed, this is borne out by the fewer fluid collections you found on CT scan, although I doubt all agree with your explanation that the difference is due to the greater mobilization required for the pancreatojejunal anastomosis. The question that still remains whether your preference is your own bias; you have shown that both are safe, the mortality is 1%. Do you prefer the gastric anastomosis?

In your presentation you emphasize pancreatic consistency: the hard and soft pancreas. I am uncertain of your definition, but I wonder whether the firm and rigid pancreas is suitable for pancreatogastrostomy?

An unusual feature of the study is the difference in incidence of biliary fistula. I find this hard to explain. In your technique, you used a tube, and I just wondered whether you felt that that silicon tube was essential; its use in the pancreatogastrostomy appears to be cumbersome. Do you feel that it is an important part of your technique?

What a physician needs to know is the long-term outlook. I have the bias, so I have no proof of it, that if you do a pancreatic gastric anastomosis, the acid, particularly with a pylorus preserving anastomosis, would immediately denature the alkaline pancreatic enzymes, leading to enzyme deficiency in the long term. Have you evidence for a difference in enzyme requirement between the groups?

Finally, I just wonder what you are going to advise from now on in your unit?

Dr. Bassi: Thank you, Dr. Russell, for your comment and question about what kind of anastomosis at the very end we prefer to carry out nowadays.

In between pancreaticojejunostomy or pancreaticogastrostomy, I think that after this study we can state that they are both safe in our hands and then be chosen depending on the anatomic conditions and underlining disease. One of the reasons for which we started to focus our interest on pancreaticogastrostomy is that we are convinced this is a good solution for the follow-up in patients with IPMT. We look after a lot of these patients and the numbers are improving. So, I cannot tell you which is better. Certainly, the data after 150 patients confirm our clinical feeling: the complicated patient with pancreaticojejunostomy goes worse than the complicated patient with pancreaticogastrostomy. Maybe another reason is that discussing these data with Dr. Yeo who experienced a similar study, we realized using 2 drains in the pancreaticojejunostomy and only one in pancreaticogastrostomy because with the same drain we can cover both the biliary and pancreatic anastomoses: less drains . . . less complications . . . who knows?

What about stenting, yes or no? In the previous study, we did with a duct to mucosa versus "classic" pancreaticoje-junostomy; we did not randomize the use of stent or not.

Looking at the "not randomized" results, we found that the stent is associated with a higher complications rate; an explanation could be that the surgeon used stents when he had problems with very small ducts. Anyway, looking at these data, we try to avoid stenting whenever possible; we stent the duct during the procedure, but we take it out afterward.

What happens from the physiopathologic point of view? When we planned this study, the gastroenterologists in Verona told me: "Claudio, do not worry, we know since the very beginning of medicine that bicarbonate is a very nice drug for the stomach; moreover, the CCK is not here and the pancreatic fluid is not activated."

We have already planned functional studies during the long-term follow-up. We will see.

Dr. Buchler: Dr. Bassi, an excellent study from Verona again, another milestone paper, that confirms what we know from the Baltimore group randomized trial. I think it has been a very good idea that you repeated this trial in Verona, and you come to the same result, that makes it much more firm that we now have 2 studies from 2 different institutions that show the same results.

My first question is: you did not say whether you tested for equal results or for superiority, so in your statistical plan did you test that pancreaticojejunostomy is better or worse or did you test for equality?

The other question is: how did you randomize the patients, because the 69 versus the 82 patients is kind of unbalanced. The third question is about the learning curve, as far as I know in Verona over 100 years you did pancreaticojejunostomy and now you ran a study with pancreaticogastrostomy, it might be that pancreaticogastrostomy is better; for example, Daniel Jaeck has published a fistula rate of 2% of pancreaticogastrostomy, so it might be that you included a learning curve of pancreaticogastrostomy in your institution. My last question is more practical, namely, you might tell us what technique you will apply in the future in Verona, the one or the other one or both the techniques.

Dr. Bassi: I will start from the end: we got the knowhow and currently we do both techniques depending on the single case. We tested the study on the basis of the Baltimore results: we were waiting for equality.

Sixty-nine in one group and 82 in another group; we randomized more than 151 patients, 12 more, 10 of these patients were in the pancreaticogastrostomy group and 2 in the pancreaticojejunostomy group. We consider these patients as dropout because they show different degrees of fibrosis by histology. Anyway, we also analyzed the data, including this group of patients, and we did not find any difference in terms of statistical significance.

The learning curve. All these operations have been carried out by 3 senior surgeons of the unit or by their personal supervision. Before we start the trial, we carried out some cases for personal training in the pancreaticogastrostomy, which usually is much easier than the pancreaticojejunostomy.

Dr. Brennan: I thought that was a terrific study, and I really enjoyed it, and actually Prof. Russell and Prof. Büchler have asked the important questions.

I just want to make a comment about your first slide, which is the Cadillac. I have never owned a Cadillac, I would like to own a Ferrari but I cannot afford it. I was most encouraged when General Motors came to Italy, but what did they did, they made an alliance with the Fiat company and I have owned a Fiat as a younger man. I eventually gave it up when I had a lot of problems; my Italian colleague asked if I knew in English what Fiat stood for, and he said "Fix it again Tony."

DR. JEEKEL: You mentioned in your introduction a few randomized studies, and one of them was the duct occlusion versus anastomosis, which we performed in Rotterdam. In the duct occlusion group, we did not perform any anastomosis. We found in the follow-up a significant higher complication rate, mostly in terms of higher incidence of postoperative diabetes.

I wondered whether you have looked at diabetes postoperatively and whether you found a difference and whether you expect when you pull through, less occlusion finally than with the duct mucosa anastomosis and maybe then less diabetes in that group.

Dr. Bassı: Thank you, Dr. Jeekel. We did not find any particular rate of diabetes in this group of patients. Maybe it should be a longer-term effect.

DR. JAECK: I enjoyed your study, and I agree with the previous comments. As Dr. Markus Büchler underlined, we reported recently a series of 250 consecutive pancreaticoduodenectomies with pancreaticogastrostomy reconstruction following the so-called Delcore procedure with invagination of the remnant pancreas into the gastric lumen [Oussoultzoglou E, et al *Arch Surg.* 2004;139:327–335]. The pancreatic fistula

rate in the pancreaticogastric anastomosis group was of 2.3%. We usually perform a rather small gastrotomy to make the pancreatic invagination tight through the gastric wall. We use a 2-layer anastomose with interrupted adsorbable suture for the seromuscular layer and a running adsorbable suture for the gastric mucosa to achieve optimal hemostasis and to avoid postoperative bleeding. Among the complications that you observed, did you register any case of gastric bleeding?

Dr. Bassi: I think this is not a big problem today. The most important thing is, on the posterior wall, to calculate the extent of the gastrotomy to telescope the pancreas in the correct amount depending on the size of the pancreas itself.

Looking in the older literature, we found that the bleeding was an important complication those days. I think that nowadays, due to improved technologies and materials as well as PPIs, we do not have these complications anymore.